

position in viral sequences within that clade. An upper case amino acid in a consensus sequence indicates that only that amino acid is found at that corresponding position in viral sequences within that clade. Strain designations with no sequence information indicate that the complete gp41 sequence has not been determined.--

Delete the fifth paragraph on page 9, lines 18-35 and insert therefor the following:

--Figures 23A to 23D present a shorthand notation of specific peptides in peptide series I through XII (as in Figure 18), indicating locking positions, amino acid substitution variant peptides, and truncation variant peptides of each. The "X" indicates a position that can be substituted with any non-helix-breaking amino acid, but preferably with an amino acid present in that position from any one of the known HIV sequences shown in Figure 16. The "B" indicates a position used for the bridging (or tethering or locking) residues. Preferred **f** positions are presented for locking; however, in less preferred embodiments the **c** and some **b** positions can be used for locking. As in Figure 18, locations of internal sequences relevant to the invention are those found between locking residues whose positions are indicated by the "|" symbols and correspond to assigned position **f**, in this example. Positions for placing either one, two or three locks in the representative presented sequences are shown. The figure delineates five **gabcde** form helical sections suitable for locking when locks occur at adjacent **f** positions. The "." indicates positions that can be optionally absent from the final constrained helical peptide compound without substantially effecting the helical properties and groove binding properties of the final constrained helical peptide. For example, a peptide based on peptide I, having the three locks placed as indicated, can optionally lack any one or all of the five N-terminal amino acids WXXWE, which are marked by a ".". Further, another series of truncated variants is indicated in

the figure--C-terminal truncated variants--since the five C-terminal residues (LWNWF) marked with a "." can be absent. When the lock is placed more centrally in the 633-678 sequence, as shown in peptide series II, peptides in this series can lack additional amino acids at the C-terminal end as indicated by the "." marked positions.--

Delete the second full paragraph on page 77, lines 5-14 and insert therefor the following:

--The peptides of the invention may further include homolog sequences of the HIV LAI strain 633-678 sequence which exhibit antiviral activity when in constrained helical form. Most preferably, the constrained peptides, when used as haptens, will generate antibodies that block viral fusion events, leading to an inhibition of viral infectivity. Such homologs are peptides whose amino acid sequences are comprised of the amino acid sequences of peptide regions of other (i.e., other than HIV-1LAI) viruses that correspond to the gp41 peptide region of 633-678. Such viruses may include, but are not limited to, other HIV-1 isolates and HIV-2 isolates. Homologs derived from the corresponding gp41 peptide region of other (i.e., non HIV-1LAI) HIV-1 isolates may include those provided in Figures 16A to 16M, or other known corresponding sequences. Particularly preferred are those derived from HIV-1SF2, HIV-1RF, and HIV-1MN, GNE6, GNE8, and Thai strain isolate A244.--

Delete the third full paragraph on page 77, lines 15-17 and insert therefor the following:

--In a particularly preferred embodiment, amino acids at positions **a** and **d** of the internal sequence of six amino acids are not amino acid substituted in the helical peptide, but are the amino acids in the known isolates or consensus sequences (see Figures 16A-16M and 17).--

Delete for the fifth full paragraph beginning on page 77, line 31 and ending on page 78, line 9 and insert therefor the following:

--Preferred compounds of the invention can include sequences from HIV-1 clade consensus sequences:

(clade B consensus) W m e W e r E I d n Y T ? l l y t L I e e s Q n Q Q e k N e q e L L e L d k W a s L w n W f (SEQ ID NO: 109);

(clade A consensus) W L q W d K E I s n Y T ? I I Y n L I E e S q n Q Q E k N E q d L L A L D K W a n L w n W F (SEQ ID NO: 110);

(clade C consensus) W M q W D R E I S N Y T d t I Y r L L E D S Q N Q Q E r N E K D L L A L D S W k N L W N W F (SEQ ID NO: 111);

(clade D consensus) W m e W E r E I d N Y T G l I Y s L I E e S Q I Q Q E K N E k e L L e L D K W A S L W N W F (SEQ ID NO: 112); and

(clade E consensus) W I E W e R E I S N Y T N q I Y e I L T e S Q n Q Q D R N E K D L L e L D K W A S L W n W f (SEQ ID NO: 113).

The amino acids in these sequences are represented by a single letter code, wherein a lower case letter is the represented amino acid or is substituted with an amino acid from that corresponding position in a sequence within the same clade, and wherein a ? is any amino acid from that corresponding position in a sequence from within the same clade. Most preferred are homologs or consensus sequences from Figures 16A-16M. The internal sequences are preferably found virus sequences in the group of HIV-1 clades consisting of clades A, B, C, D, E, F, G and F/B.--

Delete the first full paragraph on page 80, lines 7-33 and insert therefor the following:

--The amino acids in the separating sequence retain **abcdefg** assignment positions of the intervening sequence, wherein preferably the amino acids in positions **a** and **d** in the separating sequence are identical to their corresponding intervening sequence amino acids. In addition, in preferred embodiments, the amino acids in the separating sequence position **g** and **e** also are identical to their corresponding intervening sequence amino acids. Less preferably, an amino acid at any one of positions **a**, **d**, **g**, or **e** is conservatively substituted in the separating sequence (with a sequence other than that represented in the clade at that position). Most preferably, the amino acids in the separating sequence retain **abcdefg** assignment positions of the intervening sequence and an amino acid at any one of positions **a**, **d**, **g**, or **e** is substituted in the separating sequence with a corresponding amino acid from its homolog sequence from another HIV strain, from a consensus sequence of its homolog sequences from any one HIV clade, or from an amino acid substituted variant thereof. The amino acids in the separating sequence positions **b**, **c**, or **f** can be any non-helix-breaking amino acid, with the preferences given in Figures 22 and 23A to 23D. Chimeras can be formed where an amino acid at any one of positions **a**, **d**, **g**, or **e** of the internal sequence of six amino acids is substituted in the helical peptide with an amino acid from the corresponding position of a different HIV virus strain. Likewise substitutions of the same nature can be made in flanking or in separating sequences. Preferred are compounds wherein the internal amino acid sequence is from any one of the peptide sequences from Figures 23A to 23D. More preferably, the compound of the invention is selected from the group consisting of constrained helical peptides of each possible sequence having any one or any combination of